§ 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

Amendments

In the Claims:

Please cancel claims 1-13 without prejudice or disclaimer.

Please add the following new claims 14-32:

14. (New) A method of enhancing the cytotoxic sensitivity of neoplastic cells to an antifolate drug, said method comprising:

(a) delivering into said neoplastic cells a vector, said vector comprising a nucleotide molecule encoding folylpolyglutamyl synthetase (FPGS), operably linked to a promoter, wherein said FPGS is expressed in said neoplastic cells at a level higher than the endogenous FPGS level of said neoplastic cells;

(b) treating said neoplastic cells with an antifolate drug that is polyglutamated by said FPGS; and

(c) enhancing the cytotoxic sensitivity of said neoplastic cell to said antifolate drug.

15. (New) The method of claim 14, wherein said FPGS is a mammalian FPGS.

16. (New) The method of claim 15, wherein said mammalian FPGS is a human FPGS.

17. (New) The method of claim 15, wherein said antifolate drug is methotrexate, edatrexate, aminopterin, or a thymidylate synthetase inhibitor.

18. (New) The method of claim 17, wherein said antifolate drug is methotrexate or edatrexate.

19. (New) The method of claim 18, wherein said antifolate drug is edatrexate.

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20. (New) The method of claim 16, wherein said chemotherapeutic agent is methotrexate.

21. (New) The method of claim 16, wherein said chemotherapeutic agent is edatrexate.

22. (New) The method of claim 14, wherein said vector for gene delivery is a viral vector.

23. (New) The method of claim 20, wherein said vector for gene delivery is a viral vector.

24. (New) The method of claim 21, wherein said vector for gene delivery is a viral vector.

25. (New) The method of claim 22, wherein said viral vector is derived from retrovirus, adenovirus, adeno-associated virus, herpes virus, poliovirus, papillomavirus, or lentivirus.

26. (New) The method of claim 25, wherein said viral vector is derived from retrovirus, adenovirus, or herpes virus.

27. (New) The method of claim 14, wherein said vector for gene delivery is non-viral.

28. (New) The method of claim 14, wherein said vector for gene delivery is a prokaryotic vector, a cationic liposome, a fusogenic liposome, a DNA-adenovirus conjugate, a DNA-protein complex, a non-viral T7 autogene vector, a starburst polyamidoamine dendrimer, a cationic peptide, a mammalian artificial chromosome, an endothelial cell, or a macrophage.

29. (New) The method of claim 27, wherein said vector for gene delivery is a prokaryotic vector.

30. (New) The method of claim 14, wherein the vector for gene delivery is delivered into said neoplastic cells by direct injection of nucleic acid, particle-mediated gene transfer, or receptor-mediated gene transfer.

31. (New) The method of claim 14, wherein said neoplastic cells are breast cancer or colon cancer cells.

32. (New) A method of enhancing the cytotoxic sensitivity of neoplastic cells to methotrexate or edatrexate, said method comprising:

(a) delivering into said neoplastic cells a vector, said vector comprising a nucleotide molecule encoding human folylpolyglutamyl synthetase (FPGS), operably linked to a promoter, wherein said FPGS is expressed in said neoplastic cells at a higher level than the endogenous FPGS level of said neoplastic cells;

(b) treating said neoplastic cells with methotrexate or edatrexate; and

(c) enhancing the cytotoxic sensitivity of said neoplastic cell to said methotrexate or edatrexate.